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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,429	12/03/2001	Vincent Sewalt	5718-119 (035718/241421)	8554

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EXAMINER

BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 12/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/005,429

Applicant(s)

SEWALT ET AL.

Examiner

Stuart F. Baum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 62-79 and 87-94 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 62-79 and 87-94 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/30/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. The amendment filed 9/30/2004 has been entered.
2. Claims 62-79, and 87-94 are pending.
Claims 1-61 and 80-86 have been canceled.
3. Claims 62-79 and 87-94, including SEQ ID NO:13, 14, 24, and 25 are examined in the present office action.
4. Rejections and objections not set forth below are withdrawn.
5. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.
6. The application should be reviewed for errors. Errors appear, for example, in claim 87 which ends with a semicolon rather than a period.

Scope of Enablement

7. Claims 62-66 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for decreasing the number of disulfide bonds of storage proteins in a plant or part thereof comprising transforming a plant with a nucleotide sequence comprising SEQ ID NO:24, or a nucleotide sequence encoding a NADPH-thioredoxin reductase of SEQ ID NO:25, or a nucleotide sequence having at least 95% sequence identity to the coding sequence of the nucleotide sequence set forth in SEQ ID NO:24, wherein said nucleotide sequence encodes a polypeptide comprising NADPH-thioredoxin reductase activity, or a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of SEQ

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ID NO:24 under conditions specified in claim 62(d) and wherein said nucleotide sequence encodes a polypeptide comprising NADPH-thioredoxin reductase activity; and transforming said plant with a second nucleotide sequence encoding a thioredoxin h polypeptide wherein the expression of both nucleotide sequences in grains chemically reduces the disulfide bonds of storage proteins; does not reasonably provide enablement for claims drawn to a method for altering the disulfide status of storage proteins in a plant or part thereof which reads on increasing the number of disulfide bonds of a storage protein in a plant or part thereof, comprising transforming a plant with a first and second nucleotide sequence as disclosed above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicants' claims are drawn to a method for altering the disulfide status of storage proteins in a plant or part thereof comprising transforming a plant with a nucleotide sequence comprising SEQ ID NO:24, or a nucleotide sequence encoding a NADPH-thioredoxin reductase

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of SEQ ID NO:25, or a nucleotide sequence having at least 95% sequence identity to the coding sequence of the nucleotide sequence set forth in SEQ ID NO:24, wherein said nucleotide sequence encodes a polypeptide comprising NADPH-thioredoxin reductase activity, or a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of SEQ ID NO:24 under conditions specified in claim 62(d) and wherein said nucleotide sequence encodes a polypeptide comprising NADPH-thioredoxin reductase activity; and transforming said plant with a second nucleotide sequence encoding a thioredoxin h polypeptide wherein the expression of both nucleotide sequences in grains alters the disulfide status of storage proteins, or wherein the second nucleotide sequence is selected from the list of sequences disclosed in claim 63, or where the both nucleotide sequences are operably linked to a promoter.

Applicants transformed maize plants with a nucleic acid sequence of SEQ ID NO:24 encoding a NADPH-thioredoxin reductase and a nucleic acid sequence of SEQ ID NO:13 encoding thioredoxin h, both of which are operably linked to a Gamma zein promoter (page 43, lines 17 to 23). Applicants analyzed transformed plants by grinding corn kernels and treating the ground corn with 1 mM dithiothreitol (DTT) versus a control which was not treated with DTT. Applicants report that enzyme digestible dry matter percent (EDDM%) of the grain was measured using the method of Boisen and Fernandez (page 44, lines 10-13) and report that this method is a measure of digestibility (page 51, line 24). Applicants report that the digestibility of kernels overexpressing both NADPH-thioredoxin reductase and thioredoxin h is increased significantly compared to kernels from wild-type plants (page 54, lines 15-18).

Applicants' claim 62 reads on both increasing and decreasing the disulfide status of storage proteins in a plant or part thereof. Applicants have only exemplified decreasing the

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disulfide status of storage protein by overexpressing a thioredoxin h polypeptide. Applicants have not exemplified increasing the disulfide status of storage proteins by reducing the activity of endogenous thioredoxin h. Applicants' claims read on antisense technologies, or co-suppression technologies, both of which reduce the activity of thioredoxin h in a plant cell.

The state-of-the-art teach that sense and antisense constructs can behave unpredictably when transformed into a plant. Colliver et al (1997, Plant Mol. Biol. 35:509-522) showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase unexpectedly resulted in transformants with *increased* levels of chalcone synthase transcripts (page 519, left column, 2nd paragraph). Montgomery et al (Trends in Genetics, July 1998, 14(7):255-258) teach that not all transgenes can cause co-suppression in plants and that there is no basis for predicting which transgenes would have this effect (page 257, column 1, last paragraph).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:24 or 13 as probes or by designing primers to undisclosed regions of SEQ ID NO:24 or 13 and isolating or amplifying fragments, subcloning the fragments in antisense orientation or sense orientation to be used for co-suppression, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when transcribed in a plant or plant cell reduce the endogenous activity of thioredoxin h and which increases the disulfide status of storage proteins in a plant or plant part.

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Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Applicant's arguments filed 9/30/2004 have been fully considered but they are not persuasive.

Applicants contend that unlike the Colliver et al reference, Applicants' claimed invention involves expressing polynucleotides encoding NADPH-thioredoxin reductase and thioredoxin h and not polynucleotides encoding bean chalcone synthase (page 29, bottom paragraph).

Applicants contend that Colliver et al admit that their results are "not consistent with general antisense effects ..." (page 30, top paragraph). Applicants contend that antisense and co-suppression methods are known to those of ordinary skill in the art and Applicants disclose U.S. patents that disclose teachings of antisense and co-suppression (page 30, 1st full paragraph).

The Office contends that Colliver et al and Montgomery et al teach antisense and co-suppression technologies or methodologies can produce unpredictable results. The Office contends that it is irrelevant what the nucleic acids encode, but rather, that the technologies or methodologies themselves produce unpredictable results, given the lack of any disclosure by Applicants. Applicants have not taught which sequences exhibiting 95% sequence identity to SEQ ID NO:24 or 13 or which sequences that hybridize to the complement of SEQ ID NO:24 or 13 will inhibit the endogenous expression of NADPH-thioredoxin reductase or thioredoxin h when transformed into a plant. In addition, Applicants have not disclosed that inhibiting the endogenous activity of NADPH-thioredoxin reductase or thioredoxin h will increase the disulfide status of storage proteins in plants.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 62-79, and 87-94 are rejected under 35 U.S.C. 102(a) as being anticipated by Lanahan (June, 2000, WO 00/36126).

The claims are drawn to a method for altering the disulfide status of storage proteins in a plant or part thereof, a method for improving the digestibility of grain, a method for improving grain for processing or a transformed plant comprising transforming a plant with a nucleic acid sequence that hybridizes under stringent conditions, as recited in claims 62(d), 67(d), 73(d), and 87(d), to the complement of the nucleotide sequence set forth in SEQ ID NO:24 and wherein said nucleotide sequence encodes a polypeptide comprising NADPH-thioredoxin reductase activity and comprising transforming said plant with a nucleic acid sequence encoding any thioredoxin h or wherein the nucleotide sequence hybridizes under stringent conditions to the nucleotide sequence set forth in SEQ ID NO:13, wherein said part is a seed or grain, wherein the nucleotide sequences are operably linked to a constitutive, tissue preferred, or chemically regulated promoter, wherein said digestibility of said grain is increased when consumed by a ruminant or monogastric animal, wherein the grain is a maize kernel, wherein the grain is a kernel that is part of a whole corn plant harvested for silage, wherein the processing is wet

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milling, grinding, steam flaking or dry grind ethanol production, wherein the plant is a maize or soybean plant, or seed from the transformed plant.

Lanahan teaches a method of reducing the disulfide bonds in seed proteins and a plant comprising transforming corn or soybean plants with a nucleic acids encoding thioredoxin and thioredoxin reductase operably linked to a promoter and a plant comprising said sequences (pages 1-3, and page 34-35, claims 1-13). The Office interprets “thioredoxin h” and “thioredoxin” to be the same enzymes and have the same activity. The Office interprets the stated hybridization conditions to be sufficient to permit hybridization between Applicants’ sequences and the sequences of Lanahan. Lanahan also teaches that the promoter can be a constitutive promoter, a chemically-inducible promoter or a seed specific promoter (See page 11, lines 30-41, for example). The Office interprets a “seed specific” promoter to encompass a tissue preferred promoter. Lanahan discloses that the grain performance in livestock feed is increased (page 1, lines 19-22). The Office interprets the recitation “livestock” as recited on page 1, line 20, to encompass ruminant or monogastric animals. The Office interprets the recitation “grain” to include maize kernels or soybean seeds as is recited in claims 1-3 (See page 34). Because Applicants’ methods and plant all comprise the same starting materials and methods steps, then the methods of Lanahan, which also comprises the same starting material and method steps, would also improve digestibility and processing of grains, and as such, Lanahan anticipates the claimed invention. In addition, because the grain processing procedures, i.e., wet milling, grinding, steam flaking or dry grind ethanol production, all comprise the same starting materials and method steps as taught by Applicant, it would be inherent that the method

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of Lanahan would also improve the same grain processing procedures as taught by Applicant; and as such, Lanahan anticipates the claimed invention.

Applicant's arguments filed 9/30/2004 have been fully considered but they are not persuasive.

Applicants contend that the Lanahan reference which was used as a 102(e) reference in the office mailed 6/30/2004, was improper because the filing date of the Lanahan reference was prior to November 29, 2000 and it is subject to the former (pre-AIPA) version of 35 U.S.C. 102(e) (paragraph bridging pages 30 and 31 of response).

The Offices acknowledges this observation and has changed this rejection to a 102(a) rejection based on the publication date of the WO 00/36126 document.

9. No claims are allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

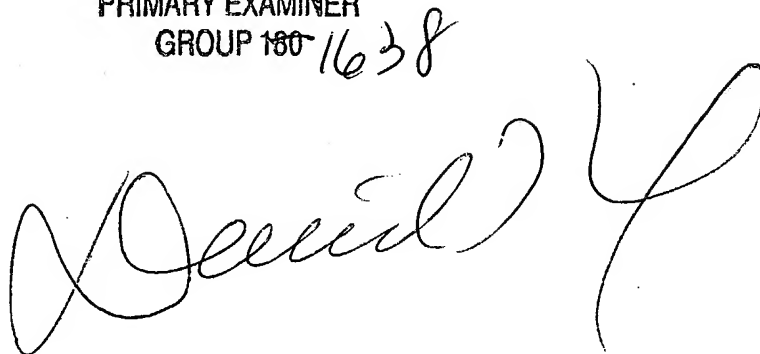
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
December 21, 2004

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180-1638

A large, stylized handwritten signature in black ink, appearing to read "David T. Fox", is written over the printed name and title of the examiner.